Stem cell based treatment strategy for Age-related Macular Degeneration (AMD)

Grant Award Details

Stem cell based treatment strategy for Age-related Macular Degeneration (AMD)

Grant Type: Disease Team Research I

Grant Number: DR1-01444

Project Objective: To develop a cellular therapy for dry Age Related Macular Degeneration (AMD) using retinal pigment epithelium (RPE) derived from human embryonic stem cells (hESC).
An important component of this approach is the use of hESC-derived RPE plated as a polarized monolayer on a synthetic substrate (rather than as a cell suspension). The substrate mimics the natural Bruch's membrane, which is important for the attachment, survival and differentiation of RPE.

Investigator:

Name:	Mark Humayun
Institution:	University of Southern California
Type:	PI

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Name:	David Hinton
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Institution:	University of California, Santa Barbara
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Name:	Pete Coffey
Institution:	Almac Diagnostics, Inc.
Type:	Partner-PI

Disease Focus: Vision Loss

Collaborative Funder: UK

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: Embryonic Stem Cell

Award Value: $18,904,916

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Final (Year 5)

View Report

Grant Application Details

Application Title: Stem cell based treatment strategy for Age-related Macular Degeneration (AMD)

Public Abstract:

Retinal degeneration represents a group of blinding diseases that are increasingly impacting the health and well being of Californians. It is estimated that by 2020, over 450,000 Californians will suffer from vision loss or blindness due to the age-related macular degeneration (AMD), the most common cause of retinal degeneration diseases in the elderly. AMD is a progressive ocular disease of the part of the retina, called the macula, which enables people to read, visualize faces, and drive. The disease initially causes distortion in central vision, and eventually leads to legal blindness.

A layer of cells at the back of the eye called the retinal pigment epithelium (RPE), provide support, protection, and nutrition to the light sensitive cells of the retina; the photoreceptors which consist of rods and cones . The dysfunction and/or loss of these RPE cells play a critical role in the loss of the PR's and hence the blindness in AMD. Effective treatment could be achieved by proper replacement of damaged RPE and retinal cells with healthy ones. More specifically, the regenerated and restored RPE layer would prevent the irreversible loss of the PR's. However, the lack of a feasible approach to restore the RPE cells has prevented the realization of a potential therapy.

Recent advances in knowledge and technology of human embryonic stem (hES) cells brings new hope for the development of cell replacement treatment. hES cells are capable of unlimited self-replication and production of different cell types. RPE cells derived from hES cells are a potentially unlimited and robust source for regenerating RPE.

We hypothesize that the dysfunction and/or loss of RPE can be overcome by regenerating and restoring the RPE through the transplantation of functionally polarized RPE monolayers derived from hES cells. Such RPE cells derived from hES can then be transplanted into the eye, using minimally invasive surgical procedures saving the PR from dying.

Our group is composed of unique multidisciplinary members who collectively have more than two decades of experience in efforts to restore sight to the blind as well as retinal cell transplantation and stem cell research. Our plan for this grant is to use our expertise and infrastructure to show to the FDA the success of our preclinical tests using hES derived RPE cells in order to get approval to conduct a clinical trial in patients at risk of vision loss due to AMD.

Statement of Benefit to California:	Age-related macular degeneration (AMD) is the leading cause of vision loss and blindness among the elderly. Based on the fact that California is one of the most populated state in the Unites States (38 million population in 2007), and a greater percentage of its population will be 65 years or older. It is estimated that over 450,000 of Californians will suffer from AMD with severe vision impairment by 2020. Even using National Eye Institute numbers from 2003 and adjusting it for the population of California, the costs for California exceed $8 billion (http://www.nei.nih.gov/eyedata/hu_estimates.asp). Since the introduction of the anti-VEGF drug Lucentis by Genentech in 2006, the cost for the treatment for AMD has even further sky rocketed. For example, the cost of these monthly injections to treat all of the new cases of neovascular (wet) AMD in 2008 in California alone would exceed 9 billion (single patient costs per year often is approximately $25k/year). Moreover, studies have shown that the devastating consequences of AMD include the progressive loss of independence and productivity, and increased risks of falls, fractures, and depression among diseased population. So this is not only a problem of the individual quality of life, but also an issue of increasing public health burden and concern. In this study, we will test the feasibility of treating AMD through the transplantation of human embryonic stem cells that have been treated to differentiate into retinal pigment epithelial cells (RPE); one of the key cell types known to primarily degenerate or die in AMD. The approach of regenerating the RPE cell layer has many advantages over regenerating photoreceptors and is much more likely to be achieved in the near future. The biggest advantage to RPE cell layer regeneration is that it is preventative and protects or rescues the photoreceptors from degenerating. Also, since it is not a neuronal cell line it does not need to form synapses with the host; a much more difficult task. The success of our preclinical experimentation with RPE replacement therapy will be seamlessly and quickly transferred into clinical trials to develop novel treatments for AMD. Ultimately, hundreds of thousands of Californians with AMD would benefit from our research, with improvement in quality of life and reduced morbidity. The California economy will significantly benefit from this work through potential reduced costs for health care and social welfare. We also envision that our research would lead to a new industry and hence many more employment opportunities and also add to the revenue generated by the state of California. Also our efforts at the University level in California would lead to new curricula in stem cells and regenerative medicine and thus educate the work force of the future.

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